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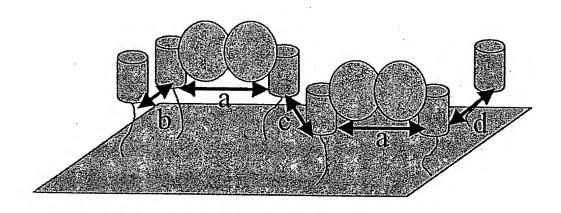
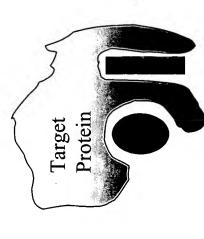
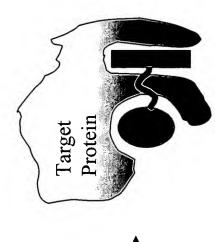


FIG. 1



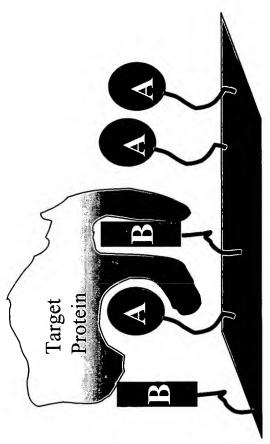
Fesik, Ellman, others



High affinity bivalent ligand

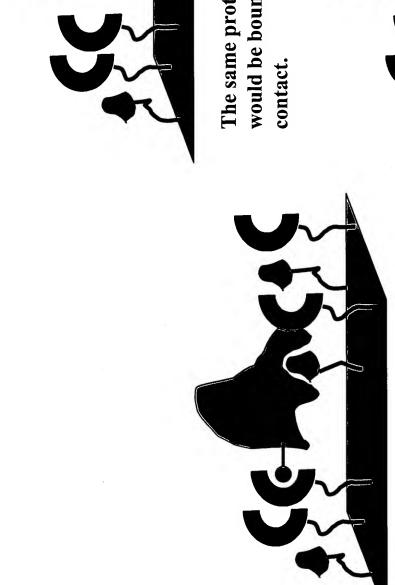
monovalent ligands

Two low affinity

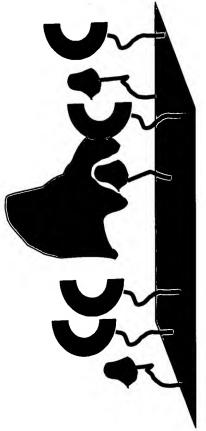


Bivalent association linked by the surface

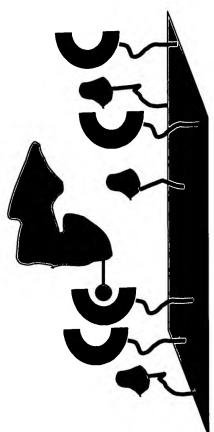
FIG. 4



High affinity binding of a particular post-translationally modified protein through a two-point contact.



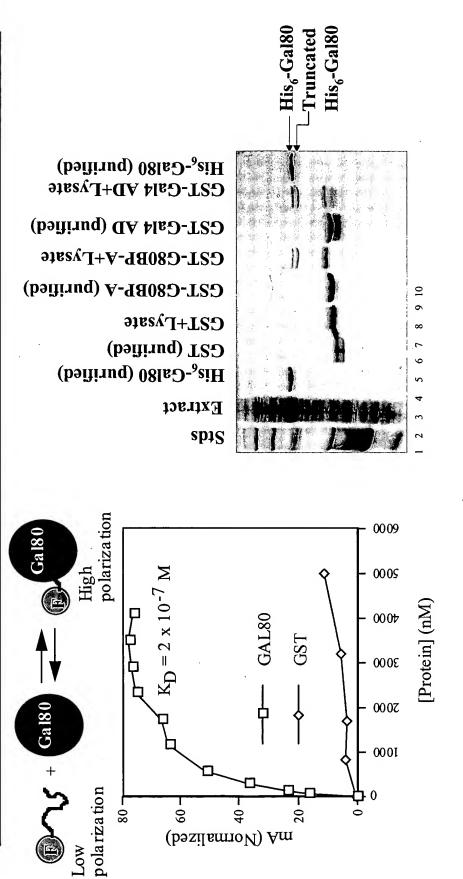
The same protein lacking the modification would be bound weakly via a one-point



Other proteins containing the same modification would be bound weakly via a one-point contact

G80BP-B: NEDWERDDQNPWDKLWMNRA G80BP-A: YDQDMQNNTFDDLFWKEGHR





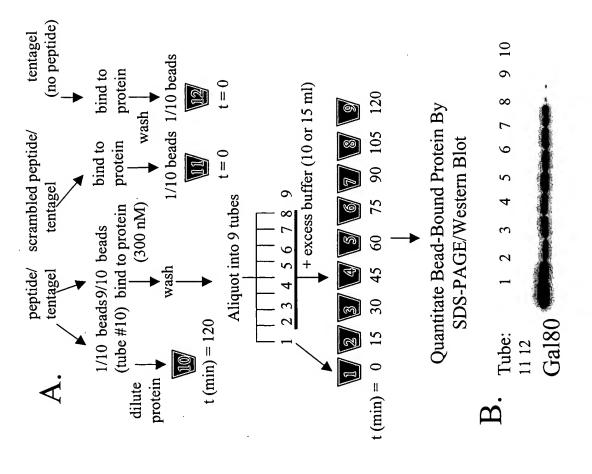


FIG. 7

A. [His6Gal80] (nM): 8 4 2 1.5 1 0.75 0.4 0.3 0.2 His6Gal80 (ng): 200 100 50 37.5 25 17.5 10 7.5 5



M.

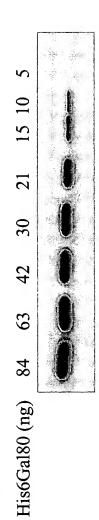


FIG. 8

FIG. 9

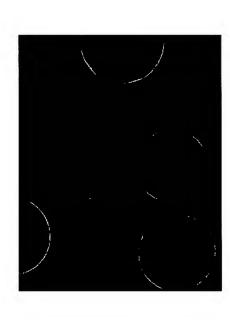


MBP-mdm2 fusion

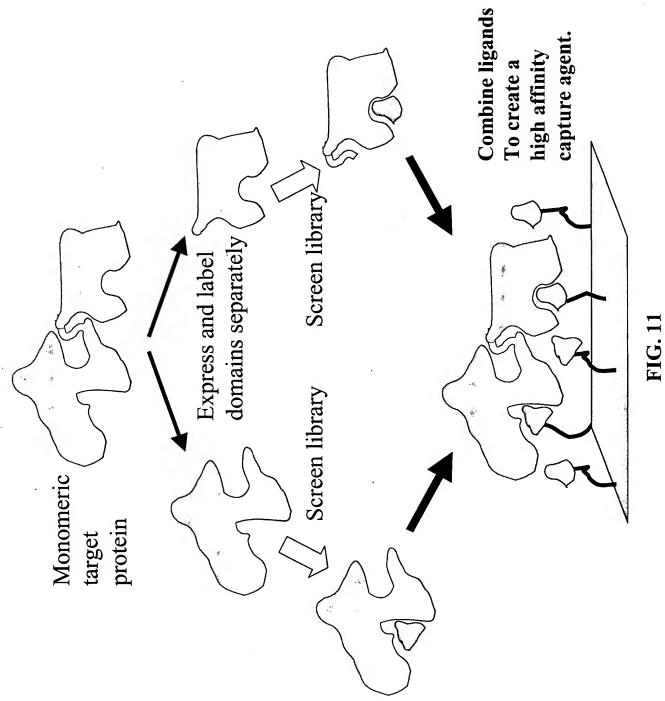
MECA ||||||

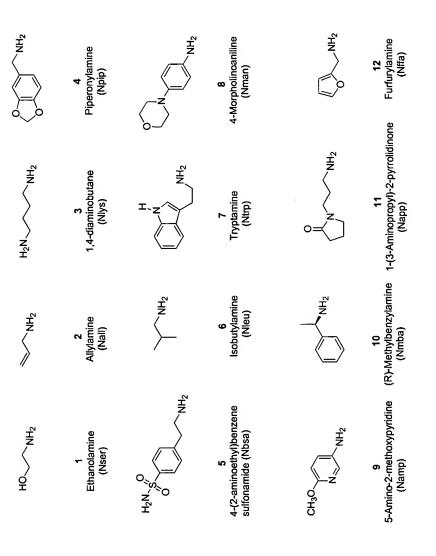
Peptides: VFFKDKKF 11111

MPRMDYWEDL 11111









13 Methoxyethylamine (Nmea)

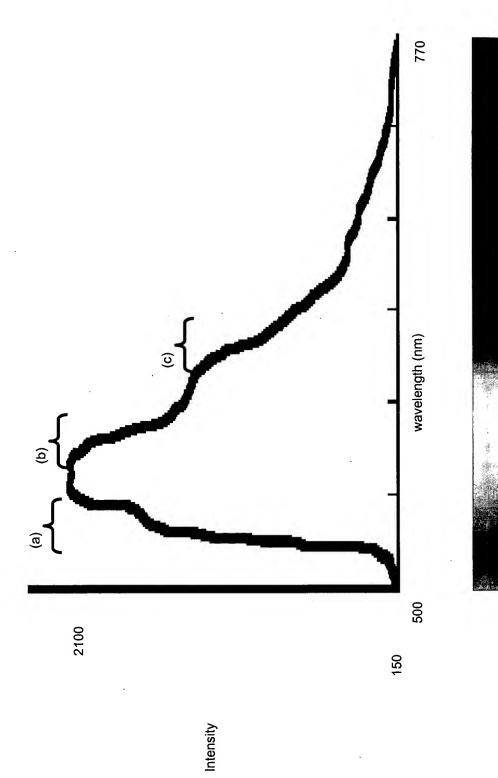
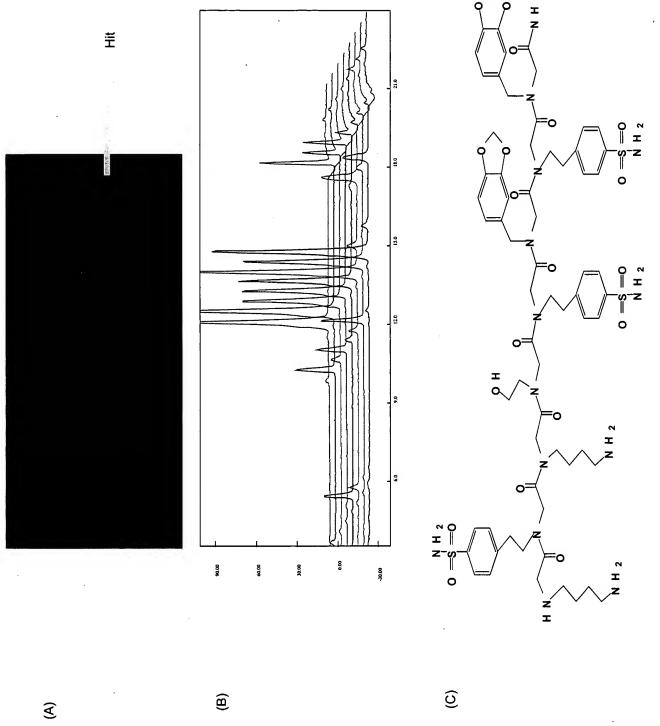


FIG. 14





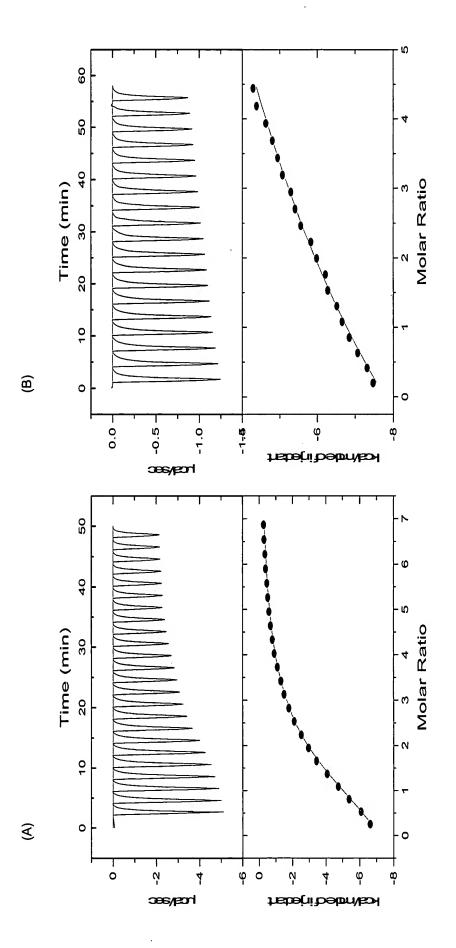


FIG. 16

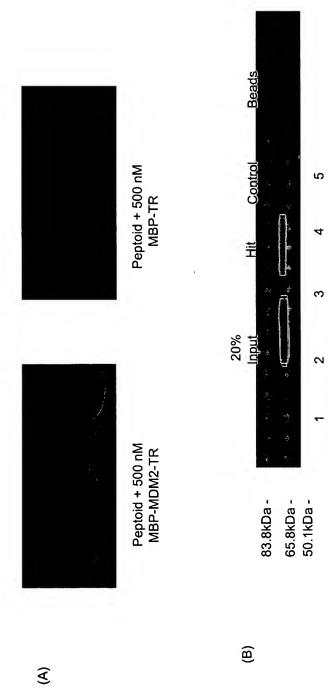
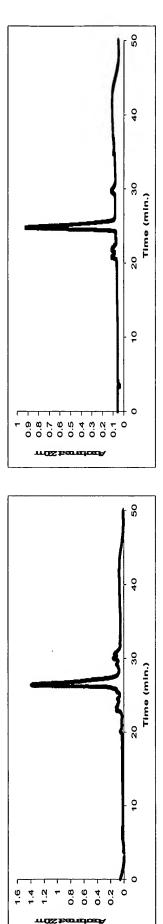
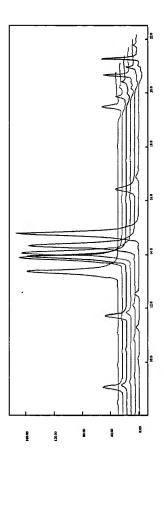


FIG. 17



Nieu-Nbsa-Niys-Napp-Ntrp-Nieu Nmba-Nieu-Napp-Nmba-Nbsa-Nffa Niys-Nmea-Ntrp-Napp-Nieu-Nieu Nmea-Npip-Nmba-Nffa-Napp-Nieu Nieu-Niys-Nmea-Nieu-Ntrp-Nmea Ntrp-Nffa-Ntrp-Nbsa-Napp-Npip Nffa-Nieu-Nmea-Npip-Niys-Nieu Npip-Nmea-Nmba-Napp-Nieu-Napp Napp-Nmea-Nmba-Npip-Nffa-Nffa

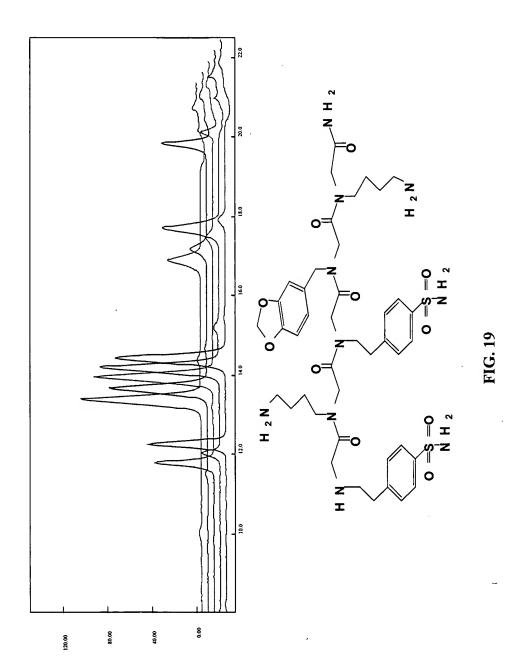
€



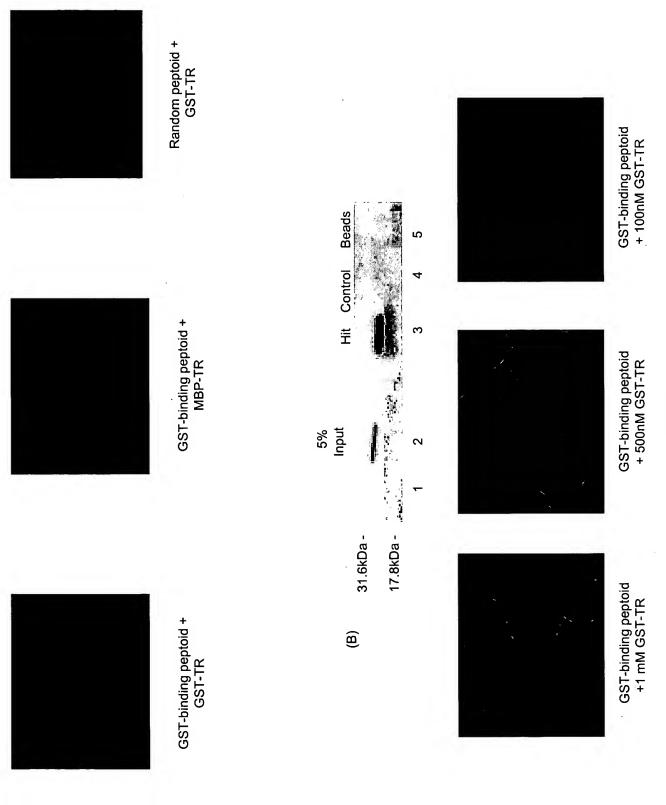
<u>@</u>

<u>O</u>

FIG. 18

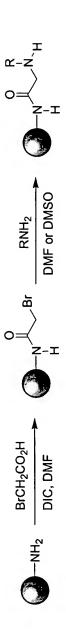


(B)



<u>ල</u>

FIG. 20



DIC: (ⁱPr)N=C=N(ⁱPr) R: any alkyl group

FIG. 21

FIG. 22

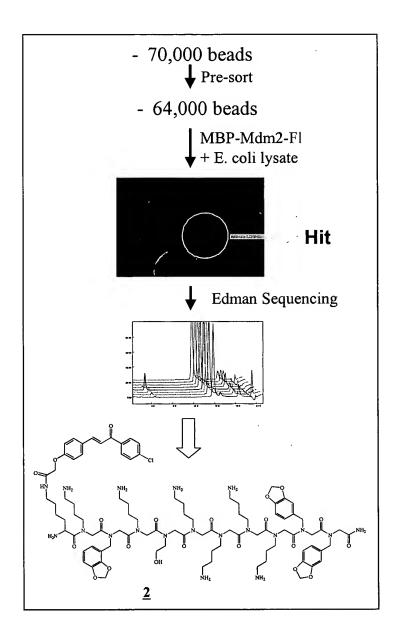


FIG. 23A-23C

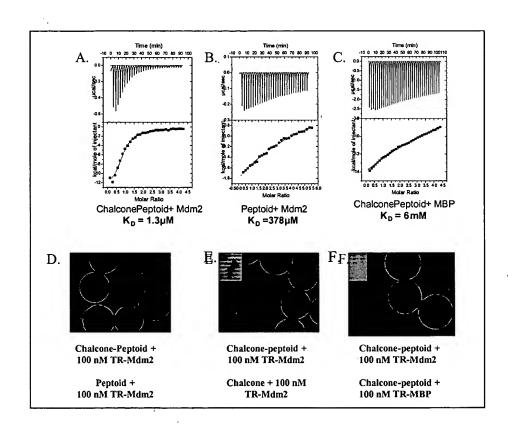


FIG. 24A-24F

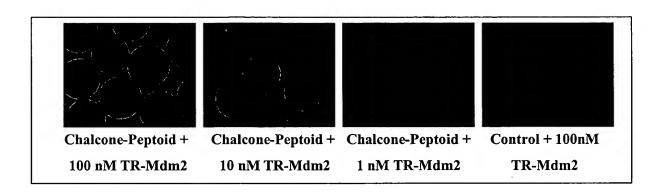


FIG 25

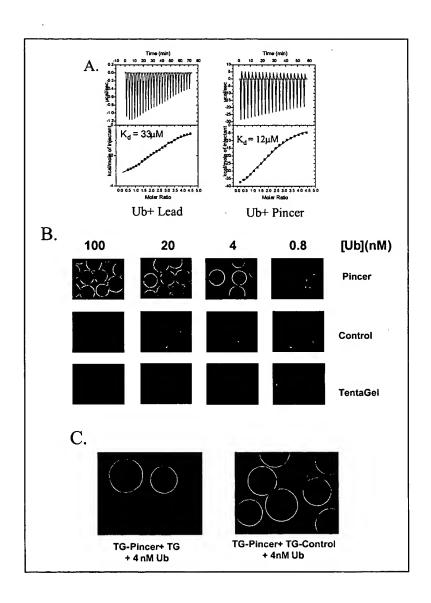


FIG. 26A-26C